

=> s separin/CN

L1 1 SEPARIN/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 351527-77-0 REGISTRY

CN **Separin (9CI)** (CA INDEX NAME)

OTHER NAMES:

CN Proteinase Esp1

CN Separase

CN Sister-sepg. protease separin

MF Unspecified

CI MAN

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

18 REFERENCES IN FILE CA (1962 TO DATE)

19 REFERENCES IN FILE CAPLUS (1962 TO DATE)

(FILE 'HOME' ENTERED AT 15:30:38 ON 20 OCT 2002)

FILE 'REGISTRY' ENTERED AT 15:31:54 ON 20 OCT 2002  
L1 1 S SEPARIN/CN

FILE 'HCAPLUS' ENTERED AT 15:32:20 ON 20 OCT 2002

FILE 'REGISTRY' ENTERED AT 15:32:23 ON 20 OCT 2002  
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L2 SEL L1 1- CHEM : 5 TERMS  
SET SMARTSELECT OFF

FILE 'HCAPLUS' ENTERED AT 15:32:24 ON 20 OCT 2002  
L3 52 S L2  
L4 21 S L3 (L) INHIBIT?  
L5 1 S L4 AND PD<19990215

FILE 'CAOLD, CAPLUS, CASREACT, CROPU, DGENE, ENCOMPPAT, ENCOMPPAT2,  
EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE,  
PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2,  
USPATFULL, USPAT2, WPIDS' ENTERED AT 15:36:32 ON 20 OCT 2002

FILE 'REGISTRY' ENTERED AT 15:36:37 ON 20 OCT 2002  
SET SMARTSELECT ON  
L6 SEL L1 1- CHEM : 5 TERMS  
SET SMARTSELECT OFF

FILE 'CAOLD, CAPLUS, CASREACT, CROPU, DGENE, ENCOMPPAT, ENCOMPPAT2,  
EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE,  
PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2,  
USPATFULL, USPAT2, WPIDS' ENTERED AT 15:36:39 ON 20 OCT 2002

L7 85 S L6  
L8 42 S L7 (L) INHIBIT?  
L9 32 DUP REM L8 (10 DUPLICATES REMOVED)  
L10 29 S L9 AND (CHROMOSOME OR CHROMATID)  
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SET SMA LOGIN

FILE 'CAPLUS' ENTERED AT 16:22:34 ON 20 OCT 2002  
L12 1 S L\*\*\*

FILE 'CAOLD, CAPLUS, CASREACT, CROPU, DGENE, DPCI, ENCOMPPAT, ENCOMPPAT2,  
EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE,  
PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2,  
USPATFULL, USPAT2, WPIDS' ENTERED AT 16:22:38 ON 20 OCT 2002

FILE 'CAOLD, CAPLUS, CASREACT, CROPU, DGENE, DPCI, ENCOMPPAT, ENCOMPPAT2,  
EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE,  
PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2,  
USPATFULL, USPAT2, WPIDS' ENTERED AT 16:23:18 ON 20 OCT 2002

L13 29 S L10

L13 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:753616 CAPLUS  
TI Proteolytic cleavage of the THR subunit during anaphase limits Drosophila separase function  
AU Herzig, Alf; Lehner, Christian F.; Heidmann, Stefan  
CS Department of Genetics, University of Bayreuth, Bayreuth, 95440, Germany  
SO Genes & Development (2002), 16(18), 2443-2454  
CODEN: GEDEEP; ISSN: 0890-9369  
PB Cold Spring Harbor Laboratory Press  
DT Journal  
LA English  
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:728178 CAPLUS  
TI Proteolysis and the cell cycle. Introduction  
AU Clarke, Duncan J.  
CS Department of Genetics, Cell Biology and Development, University of Minnesota Medical School, Minneapolis, MN, 55108, USA  
SO Cell Cycle (2002), 1(4), 233-234  
CODEN: CCEYAS; ISSN: 1538-4101  
PB Landes Bioscience  
DT Journal  
LA English  
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:726718 CAPLUS  
TI Anaphase specific auto-cleavage of separase  
AU Zou, Hui; Stemman, Olaf; Anderson, Jens S.; Mann, Matthias; Kirschner, Marc W.  
CS Department of Molecular Biology, UT Southwestern Medical Center at Dallas, Dallas, TX, 75390, USA  
SO FEBS Letters (2002), 528(1-3), 246-250  
CODEN: FEBLAL; ISSN: 0014-5793  
PB Elsevier Science B.V.  
DT Journal  
LA English

L13 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:644214 CAPLUS  
TI Regulation of human separase by securin binding and autocleavage  
AU Waizenegger, Irene C.; Gimenez-Abian, Juan F.; Wernic, Dominik; Peters, Jan-Michael  
CS Research Institute of Molecular Pathology, Vienna, 1030, Austria  
SO Current Biology (2002), 12(16), 1368-1378  
CODEN: CUBLE2; ISSN: 0960-9822  
PB Cell Press  
DT Journal  
LA English  
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:573396 CAPLUS  
DN 137:121596  
TI Compounds modulating sister **chromatid** separation and method for identifying same  
IN Peters, Jan-Michael; Waizenegger, Irene  
PA Boehringer Ingelheim International G.m.b.H., Germany  
SO Eur. Pat. Appl., 19 pp.  
CODEN: EPXXDW

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1227160	A1	20020731	EP 2001-101252	20010119
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
RE.CNT	5	THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD			
		ALL CITATIONS AVAILABLE IN THE RE FORMAT			

L13 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2002 ACS

AN 2002:548056 CAPLUS

DN 137:243836

TI The Dual Mechanism of Separase Regulation by Securin

AU Hornig, Nadine C. D.; Knowles, Philip P.; McDonald, Neil Q.; Uhlmann, Frank

CS Chromosome Segregation Laboratory, Cancer Research UK, London Research Institute, London, WC2A 3PX, UK

SO Current Biology (2002), 12(12), 973-982  
CODEN: CUBLE2; ISSN: 0960-9822

PB Cell Press

DT Journal

LA English

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2002 ACS

AN 2002:540563 CAPLUS

TI Spol3 regulates cohesin cleavage

AU Lee, Brian H.; Amon, Angelika; Prinz, Susanne

CS Center for Cancer Research, Howard Hughes Medical Institute, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

SO Genes & Development (2002), 16(13), 1672-1681  
CODEN: GEDEEP; ISSN: 0890-9369

PB Cold Spring Harbor Laboratory Press

DT Journal

LA English

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2002 ACS

AN 2002:471266 CAPLUS

TI Phosphorylation of the mitotic regulator Pds1/securin by Cdc28 is required for efficient nuclear localization of Esp1/separase

AU Agarwal, Ritu; Cohen-Fix, Orna

CS The Laboratory of Molecular and Cellular Biology, National Institutes of Health, NIDDK, Bethesda, MD, 20892, USA

SO Genes & Development (2002), 16(11), 1371-1382  
CODEN: GEDEEP; ISSN: 0890-9369

PB Cold Spring Harbor Laboratory Press

DT Journal; Miscellaneous

LA English

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2002 ACS

AN 2002:385159 CAPLUS

DN 137:211790

TI The Aurora B Kinase AIR-2 Regulates Kinetochores during Mitosis and Is Required for Separation of Homologous **Chromosomes** during Meiosis

AU Kaitna, Susanne; Pasierbek, Pawel; Jantsch, Michael; Loidl, Josef; Glotzer, Michael

CS Research Institute of Molecular Pathology (IMP), Vienna, A-1030, Austria

SO Current Biology (2002), 12(10), 798-812  
CODEN: CUBLE2; ISSN: 0960-9822

PB Cell Press

LA English  
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:86020 CAPLUS  
DN 136:212377  
TI Regulating sister **chromatid** separation by separase phosphorylation  
AU Nagao, Koji; Yanagida, Mitsuhiro  
CS Department of Biophysics, Graduate School of Science, Kyoto University, Kyoto, 606-8502, Japan  
SO Developmental Cell (2002), 2(1), 2-4  
CODEN: DCEEBE; ISSN: 1534-5807  
PB Cell Press  
DT Journal; General Review  
LA English

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2002:11853 CAPLUS  
DN 136:162818  
TI Dual inhibition of sister **chromatid** separation at metaphase  
AU Stemann, Olaf; Zou, Hui; Gerber, Scott A.; Gygi, Steven P.; Kirschner, Marc W.  
CS Department of Cell Biology, Harvard Medical School, Boston, MA, 02115, USA  
SO Cell (Cambridge, MA, United States) (2001), 107(6), 715-726  
CODEN: CELLB5; ISSN: 0092-8674  
PB Cell Press  
DT Journal  
LA English

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:786622 CAPLUS  
DN 136:98960  
TI Phosphorylation of the cohesin subunit Scc1 by Polo/Cdc5 kinase regulates sister **chromatid** separation in yeast  
AU Alexandru, Gabriela; Uhlmann, Frank; Mechtler, Karl; Poupart, Marc-Andre; Nasmyth, Kim  
CS Res. Inst. of Mol. Pathol. (IMP), Vienna, A-1030, Austria  
SO Cell (Cambridge, MA, United States) (2001), 105(4), 459-472  
CODEN: CELLB5; ISSN: 0092-8674  
PB Cell Press  
DT Journal  
LA English

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:756258 CAPLUS  
DN 136:306549  
TI Role of the kinetochore protein Ndc10 in mitotic checkpoint activation in *Saccharomyces cerevisiae*  
AU Fraschini, R.; Beretta, A.; Lucchini, G.; Piatti, S.  
CS Dipartimento di Biotecnologie e Bioscienze, Universita degli Studi di Milano-Bicocca, Milan, 20126, Italy  
SO Molecular Genetics and Genomics (2001), 266(1), 115-125  
CODEN: MGGOAA; ISSN: 1617-4615  
PB Springer-Verlag  
DT Journal  
LA English

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:749385 CAPLUS  
DN 136:321097  
TI Drosophila separase is required for sister **chromatid** separation  
and binds to PIM and THR  
AU Jager, Hubert; Herzig, Alf; Lehner, Christian F.; Heidmann, Stefan  
CS Department of Genetics, University of Bayreuth, Bayreuth, 95440, Germany  
SO Genes & Development (2001), 15(19), 2572-2584  
CODEN: GEDEEP; ISSN: 0890-9369  
PB Cold Spring Harbor Laboratory Press  
DT Journal  
LA English

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:611241 CAPLUS  
DN 135:286337  
TI Securin is not required for cellular viability, but is required for normal  
growth of mouse embryonic fibroblasts  
AU Mei, J.; Huang, X.; Zhang, P.  
CS Department of Molecular Physiology and Biophysics, Baylor College of  
Medicine, Houston, TX, 77030, USA  
SO Current Biology (2001), 11(15), 1197-1201  
CODEN: CUBLE2; ISSN: 0960-9822  
PB Cell Press  
DT Journal  
LA English

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:633401 CAPLUS  
DN 134:111149  
TI Degradation of Drosophila PIM regulates sister **chromatid**  
separation during mitosis  
AU Leismann, Oliver; Herzig, Alf; Heidmann, Stefan; Lehner, Christian F.  
CS Department of Genetics, University of Bayreuth, Bayreuth, 95440, Germany  
SO Genes & Development (2000), 14(17), 2192-2205  
CODEN: GEDEEP; ISSN: 0890-9369  
PB Cold Spring Harbor Laboratory Press  
DT Journal  
LA English

RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:252864 CAPLUS  
DN 134:160039  
TI Destruction of the securin Pds1p occurs at the onset of anaphase during  
both meiotic divisions in yeast  
AU Salah, Suhail-Maria; Nasmyth, Kim  
CS Vienna Biocenter, Institute of Biochemistry and Molecular Biology, Vienna,  
1030, Austria  
SO Chromosoma (2000), 109(1-2), 27-34  
CODEN: CHROAU; ISSN: 0009-5915  
PB Springer-Verlag  
DT Journal  
LA English

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:128329 CAPLUS  
DN 132:261134  
TI Cell cycle mechanisms of sister **chromatid** separation; roles of

AU Yanagida, Mitsuhiro  
CS Department of Gene Mechanisms, Graduate School of Biostudies, Kyoto  
University, Kyoto, 606-8502, Japan  
SO Genes to Cells (2000), 5(1), 1-8  
CODEN: GECEFL; ISSN: 1356-9597  
PB Blackwell Science Ltd.  
DT Journal; General Review  
LA English  
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:94335 CAPLUS  
DN 133:39512  
TI **Chromosome** cycle regulated by the APC/cyclosome  
AU Shirayama, Masaki  
CS Dep. Dev. Biol., Stanford Univ. Med. Cent., Stanford, CA, 94305-5329, USA  
SO Molecular Medicine (Tokyo) (2000), 37(2), 152-165  
CODEN: MOLMEL; ISSN: 0918-6557  
PB Nakayama Shoten  
DT Journal; General Review  
LA Japanese

L13 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AN 1999:470065 CAPLUS  
DN 131:240743  
TI Separating sister **chromatids**  
AU Nasmyth, Kim  
CS IMP Research Institute of Molecular Pathology, Vienna, A-1030, Austria  
SO Trends in Biochemical Sciences (1999), 24(3), 98-104  
CODEN: TBSCDB; ISSN: 0376-5067  
PB Elsevier Science Ltd.  
DT Journal; General Review  
LA English  
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 29 EUROPATFULL COPYRIGHT 2002 WILA

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

AN 1029547 EUROPATFULL ED 20000903 EW 200034 FS OS  
TIEN Pharmaceutically active compounds and method for identifying same.  
TIDE Pharmazeutische wirksame stoffe und Verfahren zu zu ihrer  
Identifizierung.  
TIFR Composes pharmaceutiques actifs et procede pour les identifier.  
IN Uhlmann, Frank, Dr., Paulusgasse 2/27, 1030 Wien, AT;  
Nasmyth, Kim, Dr., Sonnenfelsgasse 5/13, 1010 Wien, AT  
PA BOEHRINGER INGELHEIM INTERNATIONAL GmbH, Postfach 200, 55218 Ingelheim  
am Rhein, DE  
SO Wila-EPZ-2000-H34-T1b  
DS R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE;  
R IT; R LI; R LU; R MC; R NL; R PT; R SE; R AL; R LT; R LV; R MK; R RO;  
R SI  
PIT EPA1 EUROPÄISCHE PATENTANMELDUNG  
PI EP 1029547 A1 20000823  
OD 20000823  
AI EP 1999-102962 19990215  
IC ICM A61K038-55

L13 ANSWER 22 OF 29 IFIPAT COPYRIGHT 2002 IFI  
AN 10193314 IFIPAT;IFIUDB;IFICDB  
TI SECURIN IS REQUIRED FOR CHROMOSOMAL STABILITY IN HUMAN CELLS  
IN Jallepalli Prasad; Kinzler Kenneth W; Lengauer Christoph; Vogelstein Bert  
PA Unassigned Or Assigned To Individual (68000)  
PI US 2002137018 A1 20020926

FI US 2002137018 20020926  
DT Utility; Patent Application - First Publication  
FS CHEMICAL  
APPLICATION

CLMN 18  
GI 23 Figure(s).

FIGS. 1A to 1F. Generation of hSecurin<sup>-/-</sup> human cells by homologous recombination.

FIG. 1A. Schematic of knockout vector design with numbered black boxes denoting hSecurin exons.

FIG. 1B. PCR analysis of genomic DNA using STS A and STS B as primers and NEO ORF as a control.

FIG. 1C. Southern blot analysis confirms homozygous inactivation of the hSecurin locus.

FIG. 1D. Western blotting of hSecurin<sup>-/-</sup> and hSecurin<sup>+/+</sup> cell lysates with hSecurin-specific antibodies (arrows). (\*) denotes a non-specific background band.

FIG. 1E. Flow cytometry analysis of hSecurin<sup>+/+</sup> and hSecurin<sup>-/-</sup> cells

FIG. 1F. Cell cycle distribution, apoptotic fraction, and mitotic index of exponentially growing hSecurin<sup>+/+</sup> and hSecurin<sup>-/-</sup> cells.

FIGS. 2A to 2G. Chromosomal instability in hSecurin<sup>-/-</sup> cells. FISH analysis of hSecurin<sup>+/+</sup> (FIG. 2A) and hSecurin<sup>-/-</sup> cells (FIGS. 2B-E) with probes specific for **chromosome 7** (red) and **chromosome 12**

(green) (FIGS. 2A-D), or with a pan-centromeric probe (FIG. 2E). Nuclear DNA was stained with DAPI (blue). (FIG. 2F) **Chromosome** gains

and losses in hSecurin<sup>+/+</sup> and hSecurin<sup>-/-</sup> cells. The number of FISH signals per cell was determined for **chromosomes 7, 12, 17, and X**. The

fraction of cells with FISH signals equal to the modal value of two (**chromosomes 7, 12, and 17**) or the modal value of one (**X chromosome**) is highlighted in yellow. Non-modal cell populations

accounting for 5 percent or more of the total are highlighted in green (for **chromosome** gains) and red (for **chromosome**

losses). The total fraction of cells off the mode is given in the far-right column, summary of the percentage of hSecurin<sup>+/+</sup> (HCT116) and

hSecurin<sup>-/-</sup> (KO1, KO2) cells off the mode (FIG. 2G, left panel) and frequency of nuclear 'bud' structures in hSecurin<sup>+/+</sup> and hSecurin<sup>-/-</sup> cells

(FIG. 2G, right panel).

FIGS. 3A to 3D. Multiplex-FISH analysis of CIN phenotype in hSecurin<sup>-/-</sup> cells.

FIG. 3A. M-FISH karyotype from a hSecurin<sup>-/-</sup> cell metaphase.

FIGS. 3B-D. Summary of M-FISH data from parental hSecurin<sup>+/+</sup> HCT116 cells (B) and from hSecurin<sup>-/-</sup> cells (C-D). Loss of a single copy of a given

**chromosome** is marked in red, loss of both copies is marked in black, and gain of a single copy is marked in green.

FIGS. 4A to 4C. Defective execution of anaphase in hSecurin<sup>-/-</sup> cells.

FIGS. 4A-B. Time lapse microscopy of hSecurin<sup>+/+</sup> cells (A) and hSecurin<sup>-/-</sup> cells (B) stably expressing a histone H2B-GFP fusion protein. Arrows indicate aligned metaphase **chromosomes**, i.e., time 0.

FIG. 4C. Quantitative analysis of mitotic intervals in hSecurin<sup>+/+</sup> and hSecurin<sup>-/-</sup> cells.

FIGS. 5A to 5C. **Separin** regulation is defective in hSecurin<sup>-/-</sup> cells.

FIG. 5A. Lysates from HeLa cells arrested with nocodazole and released for 1.5 or 2.5 hours (left panel) and from log phase hSecurin<sup>+/+</sup> and

hSecurin<sup>-/-</sup> cells (right panel) were probed with antibodies to **separin**. The positions of the full-length (p200) and cleaved

(p60) forms of **separin** are indicated. (\*) mark a non-specific background band.

FIG. 5B. Cell cycle analysis of **separin** dynamics. hSecurin<sup>+/+</sup> cells (left panel) and hSecurin<sup>-/-</sup> cells (right panel) were synchronized

by sequential thymidine-aphidicolin blocks, released at the indicated time points, and FACS analysis was performed.

FIG. 5C. Immunoblotting of synchronized cell lysates with antibodies to **separin**, phosphorylated histone H3, cyclin B, and the CDK

**inhibitor** p21WAF1/CIP1. Full-length (p200) and cleaved p60 **separin** are indicated. (\*) indicate a non-specific band.



processing and activation of **separin** protease in vitro.  
 FIG. 6A. Immunoprecipitation of nocodazole-arrested HeLa cell and hSecurin+/+ and hSecurin-/-HCT116 cell extracts with antibodies to **separin** followed by immunoblotting before (-) and after (+) incubation in mitotic Xenopus extracts as a source of active APC (Waizenegger et al., 2000). (\*) mark a slowermigrating **separin** fragment seen in all six lanes of the in vitro assay.

FIGS. 6B-6C. **Separin** immunoprecipitates were incubated with mitotic Xenopus extracts, washed, and added to purified cohesin complexes. Samples were taken at different time points and analyzed by immunoblotting with myc antibodies. Full-length SCC1-myc migrates at 18 150 kDa; a SCC1-myc cleavage product of 110 kDa (FIG. 7B). A 55 kDa Sccl cleavage product (arrows) absent from reactions using **separin** isolated from hSecurindeficient cells (FIG. 7C).

FIG. 6D. hSecurin+/+ and hSecurin-/-HCT116 cells were transfected with Sccl-myc, nocodazole-synchronized in midmitosis, released from the nocodazole block and collected at the indicated time points. Lysates were analyzed by immunoblotting with myc antibody (top panels) and cyclin B antibody (bottom panels). Arrowhead marks the anaphase-specific 55 kDa Sccl-myc cleavage product. (\*) indicates antibody crossreacting band.

FIG. 7. Two-step 'Trigger Lock' model for the role of hSecurin in sister **chromatid** separation.

L13 ANSWER 23 OF 29 PATOSWO COPYRIGHT 2002 WILA  
 AN 2002:980642 PATOSWO ED 20020801 EW 200230 FS OS  
 TI METHOD FOR IDENTIFYING COMPOUNDS MODULATING SISTER **CHROMATID**  
 SEPARATION.  
 IN PETERS, Jan-Michael, Kiellmannseggasse 14, A-2100 Korneuburg, AT;  
 WAIZENEGGER, Irene, Lechnerstrasse 13/18, A-1030 Wien, AT;  
 SOMMERGRUBER, Wolfgang, Linzer-Strasse 19/Haus 4, A-3002 Purkersdorf, AT  
 PA BOEHRINGER INGELHEIM INTERNATIONAL GMBH, Postfach 200, 55216 Ingelheim  
 am Rhein, DE (except US);  
 PETERS, Jan-Michael, Kiellmannseggasse 14, A-2100 Korneuburg, AT (only  
 US);  
 WAIZENEGGER, Irene, Lechnerstrasse 13/18, A-1030 Wien, AT (only US);  
 SOMMERGRUBER, Wolfgang, Linzer-Strasse 19/Haus 4, A-3002 Purkersdorf, AT  
 (only US  
 SO Wila-IPA-2002-H30-T1  
 DS W AE; W AG; W AL; W AM; W AT; W AU; W AZ; W BA; W BB; W BG; W BR; W BY;  
 W BZ; W CA; W CH; W CN; W CO; W CR; W CU; W CZ; W DE; W DK; W DM; W DZ;  
 W EC; W EE; W ES; W FI; W GB; W GD; W GE; W GH; W GM; W HR; W HU; W ID;  
 W IL; W IN; W IS; W JP; W KE; W KG; W KP; W KR; W KZ; W LC; W LK; W LR;  
 W LS; W LT; W LU; W LV; W MA; W MD; W MG; W MK; W MN; W MW; W MX; W MZ;  
 W NO; W NZ; W PL; W PT; W RO; W RU; W SD; W SE; W SG; W SI; W SK; W SL;  
 W TJ; W TM; W TR; W TT; W TZ; W UA; W UG; W US; W UZ; W VN; W YU; W ZA;  
 W ZW;  
 RW AT; RW BE; RW CH; RW CY; RW DE; RW DK; RW ES; RW FI; RW FR; RW GB; RW  
 GR; RW IE; RW IT; RW LU; RW MC; RW NL; RW PT; RW SE; RW TR; RW AM; RW  
 AZ; RW BY; RW KG; RW KZ; RW MD; RW RU; RW TJ; RW TM; RW GH; RW GM; RW  
 KE; RW LS; RW MW; RW MZ; RW SD; RW SL; RW SZ; RW TZ; RW UG; RW ZM; RW  
 ZW; RW BF; RW BJ; RW CF; RW CG; RW CI; RW CM; RW GA; RW GN; RW GQ; RW  
 GW; RW ML; RW MR; RW NE; RW SN; RW TD; RW TG  
 PIT WOA2 PCT-PUBLICATION  
 PI WO 2002057566 A2 20020725  
 OD 20020725  
 AI WO 2002-EP529 20020119  
 PRAI EP 2001-101252 20010119  
 IC ICM E04F

L13 ANSWER 24 OF 29 PCTFULL COPYRIGHT 2002 Univentio  
 AN 2002076383 PCTFULL ED 20021011 EW 200240  
 TIEN SECURIN IS REQUIRED FOR CHROMOSOMAL STABILITY IN HUMAN CELLS  
 TIFR PRESENCE NECESSAIRE DE LA SECURINE POUR LA STABILITE CHROMOSOMIQUE DANS  
 LES CELLULES HUMAINES  
 IN VOGELSTEIN, Bert; KINZLER, Kenneth, W.; JALLEPALLI, Prasad; LENGAUER,  
 Christoph

AG KAGAN, Sarah, A.  
 LAF English  
 LA English  
 DT Patent  
 PI WO 2002076383 A2 20021003  
 DS AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ  
 EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR  
 LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI  
 SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW GH GM KE LS MW MZ SD  
 SL SZ TZ UG ZM ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR  
 GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN  
 TD TG  
 AI WO 2002-US6643 A 20020320  
 PRAI US 2001-09/815,340 20010323

L13 ANSWER 25 OF 29 PCTFULL COPYRIGHT 2002 Univentio  
 AN 2001088116 PCTFULL ED 20020826  
 TIEN METHOD OF MODULATING ACTIVATION OF LYMPHOCYTES VIA MODULATION OF  
 PITUITARY TUMOR TRANSFORMING GENE, RELATED SCREEINING METHODS  
 TIFR MODULATION DE L'ACTIVATION DE LYMPHOCYTES ET CRIBLAGE D'AGENTS  
 IMMUNOMODULATEURS POTENTIELS PAR CIBLAGE DE L'EXPRESSION ET/OU DE LA  
 FONCTION DU GENE DE TRANSFORMATION DE LA TUMEUR DE L'HYPOPHYSE (PTTG)  
 IN STOIKA, Rostyslav; HORWITZ, Gregory, A.; ZHANG, Xun; MELMED, Shlomo  
 PA CEDARS-SINAI MEDICAL CENTER  
 DT Patent  
 PI WO 2001088116 A2 20011122  
 DS AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE  
 ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT  
 LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
 TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ  
 BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT  
 SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG  
 AI WO 2001-US15438 A 20010512  
 PRAI US 2000-09/569,956 20000512  
 US 2000-09/687,911 20001013  
 US 2000-09/730,469 20001204  
 US 2001-09/777,422 20010205  
 US 2001-09/854,326 20010511  
 ICM C12N015-12  
 ICS A61K031-70; A61K048-00; A61K038-17; G01N033-50; A61P035-00

L13 ANSWER 26 OF 29 PCTFULL COPYRIGHT 2002 Univentio  
 AN 2001087935 PCTFULL ED 20020826  
 TIEN METHODS OF MODULATING ANGIOGENESIS BY REGULATING THE EXPRESSION OF  
 PITUITARY TUMOR TRANSFORMING GENE (PTTG)  
 TIFR PROCEDES DE MODULATION DE L'ANGIOGENESE PAR REGULATION DE L'EXPRESSION  
 DU GENE TRANSFORMANT LA TUMEUR DE L'HYPOPHYSE  
 IN HEANEY, Anthony, P.; ISHIKAWA, Hiroki; YU, Run; HORWITZ, Gregory, A.;  
 ZHANG, Xun; MELMED, Shlomo  
 PA CEDARS-SINAI MEDICAL CENTER  
 DT Patent  
 PI WO 2001087935 A2 20011122  
 DS AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE  
 ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT  
 LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
 TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ  
 BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT  
 SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG  
 AI WO 2001-US15437 A 20010512  
 PRAI US 2000-09/569,956 20000512  
 US 2000-09/687,911 20001013  
 US 2000-09/730,469 20001204  
 US 2001-09/777,422 20010205  
 US 2001-09/854,326 20010511

L13 ANSWER 27 OF 29 PCTFULL COPYRIGHT 2002 Univentio  
 AN 2001087934 PCTFULL ED 20020826  
 TIEN TREATMENT OF NEOPLASIA/TRANSFORMATION USING A PITUITARY TUMOR  
 TRANSFORMING GENE CARBOXY TERMINAL PEPTIDES  
 TIFR PEPTIDES CARBOXY-TERMINAUX DU GENE TRANSFORMANT DE LA TUMEUR DE  
 L'HYPOPHYSE (PTTG) ET LEURS PROCEDES D'UTILISATION VISANT A INHIBER UNE  
 PROLIFERATION ET/OU UNE TRANSFORMATION CELLULAIRES NEOPLASIQUES  
 IN HORWITZ, Gregory, A.; ZHANG, Xun; HEANEY, Anthony, P.; MELMED, Shlomo  
 PA CEDARS-SINAI MEDICAL CENTER  
 DT Patent  
 PI WO 2001087934 A2 20011122  
 DS AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE  
 ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT  
 LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
 TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ  
 BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT  
 SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG  
 AI WO 2001-US15254 A 20010512  
 PRAI US 2000-09/569,956 20000512  
 US 2000-09/687,911 20001013  
 US 2000-09/730,469 20001204  
 US 2001-09/777,422 20010205  
 ICM C12N015-12  
 ICS A61K048-00; A61K038-17; C12N005-10; A01K067-027; C07K016-18; A61P035-00

L13 ANSWER 28 OF 29 PCTFULL COPYRIGHT 2002 Univentio  
 \*\*\*\*\* DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L13 ANSWER 29 OF 29 USPATFULL  
 AN 2002:266283 USPATFULL  
 TI Methods of modulating angiogenesis by regulating the expression of  
 pituitary tumor transforming gene (PTTG)  
 IN Heaney, Anthony P., Los Angeles, CA, UNITED STATES  
 Ishikawa, Hiroki, Nagasaki, JAPAN  
 Yu, Run, Los Angeles, CA, UNITED STATES  
 Horwitz, Gregory A., Los Angeles, CA, UNITED STATES  
 Zhang, Xun, Malden, MA, UNITED STATES  
 Melmed, Shlomo, Los Angeles, CA, UNITED STATES  
 PI US 2002147162 A1 20021010  
 AI US 2001-777422 A1 20010205 (9)  
 RLII Continuation-in-part of Ser. No. US 2000-730469, filed on 4 Dec 2000,  
 PENDING Continuation-in-part of Ser. No. US 2000-687911, filed on 13 Oct  
 2000, PENDING Continuation-in-part of Ser. No. US 2000-569956, filed on  
 12 May 2000, PENDING Continuation-in-part of Ser. No. US 1999-894251,  
 filed on 23 Jul 1999, PENDING A 371 of International Ser. No. WO  
 1997-US21463, filed on 21 Nov 1997, UNKNOWN  
 PRAI US 1996-31338P 19961121 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 4221  
 INCL INCLM: 514/044.000  
 NCL NCLM: 514/044.000  
 IC [7]  
 ICM: A61K031-70  
 ICS: A01N043-04